Editorials

A New Clinical Investigation Section

WITH THIS ISSUE the *WJM* inaugurates a Clinical Investigation Section in affiliation with five western societies that are interested in clinical research. This section should be of particular value to those readers who are students or residents, or themselves do research. However, it is expected that each article will contain something of clinical or potential clinical interest and so should be worth the attention of virtually all of our readers. We look forward to the development of this section under the leadership of R. Paul Robertson, MD.

—THE EDITORS

Some Elements of Quality

IN THESE TROUBLED TIMES when there is so much emphasis on trying to make health care less costly or, as some might say, cheaper, physicians and the medical profession have quite properly taken the stand that while cost control is a worthy goal to be vigorously pursued, this must not be at the expense of the quality of care that is available to our patients and to the public. While it is clear the cost and quality of patient care have some relationship, it is also a fact that the costs are comparatively easy to measure whereas it has not been so easy to define or measure the quality. For this reason it is often difficult to show in what ways quality is or is not sacrificed when costs are cut. There is a pressing need to know more precisely what we are talking about when we speak of quality in patient care.

It is generally conceded that the Japanese automobile makers have found ways to make automobiles of better quality at less cost than have American manufacturers. Given the many reasons for their lower costs (some of which are obvious and some probably not so obvious), one may then ask how they make sure of the quality of their product. It has been said that the Japanese automobile makers have identified four elements that should be present in the manufacturing process to assure quality. These are (1) standards, (2) performance, (3) accountability and (4) something that might be called esprit de corps or a sense of group pride in the quality of the product. Apocryphal as this may be, perhaps something can be learned from it about how to tell better whether quality is or is not present in patient care as this is rendered under one or another economic arrangement.

Standards. We have already in place a relatively sophisticated system of standards for professional education (accreditation and certification), for drugs and equipment (FDA) and for hospitals and health care institutions (JCAH and licensure). We are beginning to develop generally accepted standards for the therapy of some conditions such as hypertension and diabetes mellitus. As the scientific data bases improve it may be expected that there will be more accepted standards for the treatment of more conditions. So it is indeed true that the medical profession has its standards and that they are high. It is only to be hoped that they will not be too seriously eroded by antitrust or other shortsighted actions by governments, courts or anyone else.

Performance. Over the years the medical profession has been increasingly concerned about performance in patient care. It began with tissue committees in hospitals which sought to relate surgical procedures to outcomes. More recently other forms of peer review have become commonplace, especially in hospital settings. The harsh realities of successful malpractice actions, both justified and not so justified, have focused greater attention on practice performance. So far it has been difficult to apply peer review to practice performance in physicians' offices outside of a hospital, clinic or a group practice. While the medical profession has been a leader among the professions in developing peer review of practice performance, its monitoring of professional performance certainly does not match the monitoring of the performance of the workers that is done to assure quality in a Japanese automobile. We are probably only at the beginning of what needs to be done in peer review of practice performance by physicians and other health professionals if we are to be able to measure and assure the quality of care rendered in the different economic arrangements that are coming into being.

Accountability. Accountability is a step beyond actual performance. It requires data to support what is done. To the extent that medical practice is an art this accountability is difficult; to the extent that it is a science data can be developed so as to make it accountable. The science of accountability in medical practice and patient care is in its infancy, yet it seems essential that this be developed if we are to know whether or not there is quality in patient care rendered in different settings.

Esprit. Esprit is something more readily sensed than measured. One senses that it is now usually present in good measure among health care providers, in health care institutions and in the health care teams that give care to patients. But one also senses that this esprit may be fragile and become threatened in circumstances where harsh competition displaces an atmosphere of cooperation and close collaboration, or when unwanted or poorly understood policy decisions are made by far-off governments or some sort of absentee corporate landlords. Although difficult to measure, esprit or pride in workmanship among physicians and other health care providers is an essential element in the quality of patient care.

At this moment the powers that be in government and elsewhere are giving lip service to maintaining quality

while trying desperately to reduce costs in health care. Perhaps this is all that can be expected until exactly what is meant by quality becomes more tangible and more visible for all to see. Clearly this urgently needs more attention by the medical profession. There just might be a lesson to be learned from the apocryphal Japanese automakers' attention to standards, performance, accountability and esprit among workers to assure quality in spite of lower costs. —MSMW

Chemicals and the Development of Cancer

IN THE PAST TWO DECADES a radical change in the perception of cancer by the medical profession and by the public at large has occurred. From a disease almost universally viewed as being of unknown origin or causation some three decades ago, cancer has become perceived today as *the* ultimate expression of environmental contamination. This extreme view is very widely held but is perhaps only partially valid.

As clearly stated by Smuckler in this issue and in other recent reviews,[1-4] many epidemiologic studies, backed by an increasing body of experimental work, have implicated a variety of chemicals (some 30-odd), some viruses and several forms of irradiation, as initiating causes of human cancer. Many cancers of the respiratory tract and some of the genitourinary system, upper gastrointestinal tract, skin and thyroid have environmental components, often chemicals, as important etiologic agents. This has naturally led to the popular thesis that a major advance in cancer prevention will rapidly occur when the offending environmental agents are identified and removed. This is no doubt true in some instances—for instance, smoking and lung cancer, certain chemicals and bladder cancer, vinyl chloride and thorotrast and angiosarcoma of the liver, asbestos and mesothelioma—to name some of the more obvious examples. The exposures to the chemicals in these instances are often intensive or prolonged, or both.

Yet research in the past decade or so has been toward a major modification of this viewpoint, namely that *exposure* to a carcinogen is by no means synonymous with induction of cancer and that the presence of the carcinogen in the environment is but one factor in a multifactorial matrix or network. Although we now appreciate more readily the complex multistep nature of the very long "preneoplastic" or "precancerous" stages in cancer development with chemicals and other agents, evidently even for the very early steps of initiation, such a perspective is more realistic and valid than is the previous simple equation of exposure and risk.

There are at least five interacting segments of a network that determine what effect a certain exposure to a carcinogen might have on initiating the carcinogenic process: (1) concentration and duration of exposure to the carcinogens; (2) the efficiency with which a chemical is metabolized to an active carcinogen or to noncarcinogenic derivatives; (3) the efficiency with which the target tissue cells are able to "detoxify" carcinogens; (4) the presence and rate of repair of chemical and physical damage to DNA,[2] and (5) the presence or induction of cell proliferation in target cells.

1. A clear-cut dose response is seen in many instances with chemical carcinogens in humans. For example, with smoking and with occupational exposure to aromatic amines (benzidine, β-naphthylamine), vinyl chloride and the like, a relationship between levels of exposure, duration of exposure and cancer incidence has been documented. With the large number of carcinogens that are found in our environment, however, the dose range is often quite low. Under such circumstances, the other four known factors almost certainly play a determinant role.

2. The metabolic capability for different carcinogens (or, more accurately, "procarcinogens") varies enormously from tissue to tissue and species to species. In general, humans are quite capable of metabolizing many procarcinogens of different types to active carcinogenic derivatives.[1,2] The variations in this capacity are no doubt an important factor in determining the organ sites for different carcinogens.

This component of the network is modulated by diet, hormones and genetics. Major positive or negative influences on metabolic activation can be shown for each of these three major types of modulators in animals. Conceivably, the known effects of diet, hormones and genetics on human cancer incidence may be exerted in part on this aspect of carcinogenesis.

3. A factor that is now receiving increasing attention is the efficiency with which cells or tissue can "soak up" or inactivate activated forms of carcinogens. Glutathione and the enzymes glutathione-S-transferase, epoxide hydrolase and glucuronyl transferase, among others, are able to convert active carcinogens to various conjugated forms or to hydrated forms, steps that lead either directly or indirectly to inactivation.[5] Each tissue has a constellation of enzymes and other components that can readily inactivate active derivatives of potential carcinogens, mutagens and other xenobiotics. Such reactions have been shown to protect cells against damage to DNA and other macromolecules by carcinogens.

4. The efficiency by which damage to DNA is repaired is a critical factor in the genesis of epidermoid carcinoma and melanoma by ultraviolet light in humans (for example, xeroderma pigmentosum). Conceivably the same might also be operating for chemical carcinogens, because virtually every tissue has a spectrum of "repair enzymes." The exact role of such repair activity in the genesis of cancer by chemicals in humans has yet to be delineated.

5. Cell proliferation is known to be an essential step in the initiation of carcinogenesis with chemicals and probably also with some viruses and radiations. In the liver, pancreas, urinary bladder and other adult "quiescent" tissues, there is good evidence that local tissue damage (such as toxic hepatitis) plays an essential role in starting the carcinogenic process. The tissue damage leads to local cell proliferation and the latter is required